REMARKS

Favorable reconsideration of this application as presently amended is respectfully requested. Claims 1-6, 8-48, 51 and 53-57 are pending. Claims 14 and 18-47 are withdrawn from consideration, claims 49, 50 and 52 are canceled and claims 1 and 48 are amended. No new matter is added.

Support for the amendments to the claims may be found in the specification at page 6, lines 15-16; page 8, lines 26-27; Example 4; as well as elsewhere throughout the original specification, claims and figures.

Claims 48, 49 and 51 stand rejected under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,583,010 to Baumbach *et al.* This rejection is respectfully traversed with respect to the claims as currently presented.

Claim 48 recites a method for non-cellular display of 7-transmembrane receptors comprising a) incorporating an attachment means to a receptor; b) solubilizing the receptor; c) presenting the receptor in conjunction with a support; d) presenting at least one ligand to bind to the receptor, wherein said ligand is known to bind to the receptor; e) combining the receptor and ligand to accomplish binding while the receptor is bound to the support; and f) sorting the bound receptor ligand pairs by fluorescence and using flow cytometry to analyze the fluorescence and binding interactions in real-time.

At a minimum, Baumbach fails to teach using flow cytometry to analyze the fluorescence and binding interactions in real-time. As admitted at page 5, line 3, of the Office Action, Baumbach is silent with regard to flow cytometry. Thus, Baumbach does not teach or suggest all of the features of claim 48. Therefore, claim 48 is patentable over Baumbach. Applicants respectfully request reconsideration and

withdrawal of this rejection.

The cancellation of claim 49 has obviated the rejection of that claim. Claim 51 depends directly from claim 48, and, accordingly, includes all of the patentable features of claim 48 as well as other patentable features. Therefore, claim 51 is patentable over Baumbach for at least the reasons discussed above with respect to claim 48.

Claims 1, 6, 9-13, 15-17, 50, 52 and 53-57 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of U.S. Patent No. 5,583,010 to Baumbach *et al.* with U.S. Patent No. 5,639,603 to Dower *et al.* This rejection is respectfully traversed with respect to the claims as currently presented.

Claim 1 as amended claims a method for non-cellular analysis and display of 7-transmembrane receptors comprising a) incorporating an attachment tether to a receptor; b) solubilizing the receptor; and c) presenting the receptor in conjunction with a support, wherein said support comprises at least one substrate selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry, and wherein the receptor in conjunction with a support is analyzed with a flow cytometer in real-time. However, at a minimum, the references fail to teach or suggest analyzing with a flow cytometer in real-time as recited in claim 1, and therefore; claim 1 is patentable over Baumbach and Dower, alone or in combination.

As admitted in the Office Action at page 5, line 3, Baumbach is silent with regard to flow cytometry. Thus, Dower is cited for teaching the general applicability of flow cytometry to the sorting of receptors and bound ligands. However, the general methodology and the flow cytometric analysis of Dower is very different from that recited in claim 1.

Dower provides for solubilization of a molecular or ligand library and display of the library on beads. The bead-bound library is then placed in contact with labeled receptors. A washing step is employed to remove unbound or non-specifically bound receptors. Then, a flow cytometer is used to identify and isolate individual beads showing high fluorescence. *See*, Dower, Col. 31, line 42+.

Claim 1 differs in several respects. Dower solubilizes and binds a ligand library to a bead. However, claim 1 recites the solubilization and subsequent attachment via a tether of a receptor to a bead. The solubilization and binding of the receptor allows the flow cytometric analysis to be carried out in real-time (*i.e.*, without the need for a washing step.) On the other hand, the binding of receptors in solution to an unknown ligand library discussed in Dower, requires a washing step to remove unbound or non-specifically bound receptors before analyzing with a flow cytometer. This extra step (or steps) adds time and the possibility for error in the analysis step. Through this process, Dower seeks to determine the identity of the bound ligand within the ligand library and thus seeks the areas of high fluorescence for isolation. However, in claim 1, it is a known receptor that is bound to the bead and it is the interaction with the bound receptor that is analyzed.

Thus, as shown above, Baumbach and Dower, alone or in combination, fail to teach or suggest every feature of claim 1. Therefore, claim 1 is patentable over the combination of Baumbach and Dower. Thus, Applicants respectfully request reconsideration and withdrawal of the rejection.

The cancellation of claims 50 and 52 has obviated the rejection of those claims. Claims 6, 9-13, 15-17 and 53-57 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 6, 9-13, 15-17 and 53-57 are patentable over the combination of Baumbach and Dower for at least the reasons discussed above

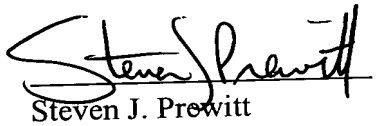
with respect to claim 1.

Claims 2, 3-5 and 8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over the combination of U.S. Patent No. 5,583,010 to Baumbach *et al.* with U.S. Patent No. 5,639,603 to Dower *et al.* and further in view of Robeva, AS *et al.*, *Drug Development Research*, 39 (243-252) 1996. This rejection is respectfully traversed with respect to the claims as currently presented.

Claims 2, 3-5 and 8 depend directly or indirectly from claim 1, and, accordingly, include all of the patentable features of claim 1 as well as other patentable features. Therefore, claims 2, 3-5 and 8 are patentable over the combination of Baumbach and Dower and further in view of Robeva for at least the reasons discussed above with respect to claim 1.

If the Examiner has any questions or concerns regarding the present response, the Examiner is invited to contact Steven J. Prewitt at 703-591-2664. In view of the foregoing, it is respectfully submitted that this application is in condition for allowance, and favorable action is respectfully solicited.

Respectfully submitted,



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August 21, 2002

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	)	
	)	
SKLAR *et al.*	)	**Examiner: Brannock, M.**
	)	
Serial Number: 09/370,358	)	**Art Unit: 1646**
	)	
Filed: August 9, 1999	)	
	)	
For: DISPLAY OF RECEPTORS AND ANALYSIS OF BINDING INTERACTIONS AND DRUG LIBRARIES	)	**Docket No.: UNME-0078-1**

Director of the U.S. Patent and Trademark Office
Washington, D.C. 20231

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Sir:

Below are the amendments in the accompanying Amendment for the above-identified application shown in redlined format:

IN THE CLAIMS

Please cancel claims 49, 50 and 52 without prejudice or disclaimer.

Please amend the claims, without prejudice or disclaimer, as indicated below:

1. (Twice Amended) A method for non-cellular analysis and display of 7-transmembrane receptors comprising the following steps:

a) incorporating an attachment tether to a receptor;

b) solubilizing the receptor; and

c) presenting the receptor in conjunction with a support, wherein said support comprises at least one substrate selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry, and wherein the receptor in conjunction with a support is analyzed with a flow cytometer in real-time.

2. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating at least one of the following tags from the group

consisting of C-Histidine, N-Histidine, biotin, and GST tags.

3. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating a tag into an oligonucleotide.

4. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating a tag into a GPCR construct prior to amplification.

5. The method of claim 1 wherein the step of solubilizing the receptor comprises solubilizing by lysing cell membranes containing the receptor.

6. The method of claim 1 wherein the step of presenting the receptor in conjunction with a support comprises presenting by affinity coupling the receptor to a particulate substrate.

8. The method of claim 1 wherein the step of presenting the receptors in conjunction with a support comprises presenting on a support comprising a Ni^{2+} silica bead.

9. The method of claim 1 wherein the step of presenting the receptors in conjunction with a support comprises presenting a fluorescently labeled receptor.

10. The method of claim 1 further comprising the step of (d) presenting at least one ligand to bind to the receptor, wherein said ligand is known to bind to the receptor.

11. The method of claim 10 wherein the step of presenting at least one ligand to bind to the receptor comprises presenting at least one fluorescently labeled ligand.

12. The method of claim 10 wherein the step of presenting at least one ligand to

bind the receptor comprises presenting a library of ligands.

13. The method of claim 10 wherein the step of presenting at least one ligand to bind the receptor comprises presenting at least one ligand on a support.

15. The method of claim 10 further comprising the step of (e) combining the receptor and ligand to accomplish binding.

16. The method of claim 15 further comprising the step of (f) sorting the bound receptor ligand pairs by fluorescence.

17. The method of claim 16 wherein the step of sorting the bound receptor ligand pairs by fluorescence comprises sorting the bound receptor ligand pairs by flow cytometry.

48. (Amended) A method for non-cellular display of 7-transmembrane receptors comprising the following steps:

a) incorporating an attachment means to a receptor;

b) solubilizing the receptor; ~~and~~

c) presenting the receptor in conjunction with a support;

d) presenting at least one ligand to bind to the receptor, wherein said ligand is known to bind to the receptor; ~~and~~

e) combining the receptor and ligand to accomplish binding while the receptor is bound to the support; and

f) sorting the bound receptor ligand pairs by fluorescence and using flow cytometry to analyze the fluorescence and binding interactions in real-time.

51. The method of claim ~~49~~48, wherein said step of sorting the bound receptor pairs by fluorescence is carried out while the receptor is bound to the support.

53. The method of claim 48, wherein said support comprises at least one substrate

selected from the group consisting of silica bead substrates, latex bead substrates and other bead substrates appropriate for flow cytometry.

54. The method of claim 1 wherein the step of incorporating an attachment tether to a receptor comprises incorporating at least one epitope tag.

55. The method of claim 54 wherein said at least one epitope tag is an N-terminal tag.

56. The method of claim 54 wherein said at least one epitope tag is a C-terminal tag.

57. The method of claim 54 wherein said at least one epitope tag is an internal tag.